PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing: 10 January 2002 (10.01.02)	
International application No.: PCT/GB00/03280	Applicant's or agent's file reference: P24404/PPP
International filing date: 29 August 2000 (29.08.00)	Priority date: 28 August 1999 (28.08.99)
Applicant: STRACHAN, John, Scott	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International preliminary Examining Authority on:

27 February 2001 (27.02.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer: J. Zahra
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

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COMMUNICATION OF
INTERNATIONAL APPLICATIONS

(PCT Article 20)

To:

Commissioner
US Department of Commerce
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Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as designated Office

Date of mailing:
04 December 2001 (04.12.01)

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:	International publication no.:
PCT/GB00/03280	

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

Copy for the elected Office (EO/US)

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

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COMMUNICATION IN CASES FOR WHICH NO OTHER FORM IS APPLICABLE

To:

PACITTI, Paolo
Murgitroyd & Company
373 Scotland Street
Glasgow G5 8QA
ROYAUME-UNI

Date of mailing (*day/month/year*) 03 December 2001 (03.12.01)	
Applicant's or agent's file reference P24404/PPP	**REPLY DUE** see paragraph 1 below
International application No. PCT/GB00/03280	International filing date (*day/month/year*) 29 August 2000 (29.08.00)
Applicant STRACHAN, John, Scott	

1. ☐ REPLY DUE within _____ months/days from the above date of mailing

☐ NO REPLY DUE, however, see below

☒ IMPORTANT COMMUNICATION

☐ INFORMATION ONLY

2. COMMUNICATION:

The International Bureau regrets to inform the applicant that, due to a clerical error, the above identified international application has not been published promptly after the expiration of 18 months from the priority date, as provided in PCT Article 21(2)(a).

International publication will now take place on 10 January 2002 (10.01.02).

Meanwhile, the International Bureau will communicate a copy of the international application to each designated Office, in accordance with PCT Article 20.

A copy of this notification has been sent to the receiving Office RO/US and all designated Offices.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer R. Chrem
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

Form PCT/IB/345 (July 1992)

Kevin's copy

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For Receiving Office use only

PCT/GB 00 / 03280
International Application No.

29 AUG 2000 29.08.2000
International Filing Date

United Kingdom Patent Office
PCT International Application
Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) P24404/PPP

*TITLE has changed, please see sheet

Box No. I TITLE OF INVENTION

*C "Molecular Resonance"

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

STRACHAN John Scott
6 Marchhall Crescent
EDINBURGH
EH16 5HN
GB

[X] This person is also inventor.

Telephone No.
--

Facsimile No.
--

Teleprinter No.
--

State *(that is, country)* of nationality:
GB

State *(that is, country)* of residence:
GB

This person is applicant for the purposes of: [X] all designated States [ ] all designated States except the United States of America [ ] the United States of America only [ ] the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

ADDED RO/GB

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
[ ] applicant only
[ ] applicant and inventor
[ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: [ ] all designated States [ ] all designated States except the United States of America [ ] the United States of America only [ ] the States indicated in the Supplemental Box

[ ] Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: [X] agent [ ] common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

PACITTI Paolo
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373 Scotland Street
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GB

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Teleprinter No.
--

[ ] **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a)(*mark the applicable check-boxes; at least one must be marked*):

Regional Patent

☒ **AP** **ARIPO Patent:** **GH** Ghana, **GM** Gambia, **KE** Kenya, **LS** Lesotho, **MW** Malawi, **MZ** Mozambique, **SD** Sudan, **SL** Sierra Leone, **SZ** Swaziland, **TZ** United Republic of Tanzania, **UG** Uganda, **ZW** Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☒ **EA** **Eurasian Patent:** **AM** Armenia, **AZ** Azerbaijan, **BY** Belarus, **KG** Kyrgyzstan, **KZ** Kazakstan, **MD** Republic of Moldova, **RU** Russian Federation, **TJ** Tajikistan, **TM** Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** **European Patent:** **AT** Austria, **BE** Belgium, **CH and LI** Switzerland and Liechtenstein, **CY** Cyprus, **DE** Germany, **DK** Denmark, **ES** Spain, **FI** Finland, **FR** France, **GB** United Kingdom, **GR** Greece, **IE** Ireland, **IT** Italy, **LU** Luxembourg, **MC** Monaco, **NL** Netherlands, **PT** Portugal, **SE** Sweden and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ **OA** **OAPI Patent:** **BF** Burkina Faso, **BJ** Benin, **CF** Central African Republic, **CG** Congo, **CI** Côte d'Ivoire, **CM** Cameroon, **GA** Gabon, **GN** Guinea, **GW** Guinea Bissau, **ML** Mali, **MR** Mauritania, **NE** Niger, **SN** Senegal, **TD** Chad, **TG** Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (*if other kind of protection or treatment desired, specify on dotted line*).....

National Patent(*if other kind of protection or treatment desired, specify on dotted line*):

☒	AE	United Arab Emirates	☒	KZ	Kazakhstan
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☒	KR	Republic of Korea			
☒	KZ	Kazakhstan			

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

☐ .....

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of .....

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.

(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit).

PCT/GB 00 / 03280

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 28 AUGUST 1999 28.08.99	9920351.5	GB		
item (2)				
item (3)				

ADDED RO/GB

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used)* : ISA /

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority)*:

Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets**:

request	: 3
description (excluding sequence listing part)	: 22
claims	: 4
abstract	: 1
drawings	: 7
sequence listing part of description	:
Total number of sheets	: 37

This international application is **accompanied by** the item(s) marked below:

1. ☐ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify)*: Paents Form 23/77

Figure of the drawings which should accompany the abstract: 1

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

(Murgitroyd & Company

For receiving Office use only

1. Date of actual receipt of the purported international application: 29 AUG 2000 29.08.2000	2. Drawings: ☒ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. ☒ Transmittal of search copy delayed until search fee is paid.

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Date of receipt of the record copy by the International Bureau: 13 SEPTEMBER 2000 (13.09.00)

Molecular Resonance

The present invention relates to molecular resonance of molecules, in particular molecular resonance generated by laser radiation.

The concept of introducing high Q molecules that may be stimulated by laser light to deliver toxic or therapeutic effects is known from Dunlavy US5313315. However, the direct stimulation of natural biological processes by means of molecular resonance using modulated or selective wavelength lasers has hitherto proved to be impossible. This is because of the scattering nature of the medium, the close proximity of many resonances in natural molecules and the difficulty of differentially raising the temperature and thereby the reactivity of individual desired molecules.

The present invention defines an apparatus and method which overcomes some of these problems and covers the nature and type of molecule susceptible to differential stimulation.

Many critical chemical reactions in the body are functions of the Cell Surface Cell Adhesion Molecules that are in turn moderated by various integrins. The geometric structure of many Cell Adhesion Molecules and particular integrins is such that they are capable of supporting a resonance at relatively low frequency and surprisingly high Q. Unlike most protein structures which are heavily damped or inherently rigid in structure these molecules generally take the form of a pair of relatively rigid structures separated by space often bridged by a single strand. This structure is especially sensitive to periodic stimulation by a laser source especially when the molecule surface is neutral or slightly negatively charged. The polar and hydrophobic regions of the molecule also differentially absorb energy from laser light. This causes brief alterations in both the structural bond energy and consequently tends to amplify the vibration of the molecule. The effect of this is to slightly increase the chemical reactivity of particular molecules on a cell surface relative to the surrounding molecules of a more generally damped structure or other high Q molecules of a different resonant frequency.

In vivo the scattering of light at suitable excitation wavelengths is extreme and as a result even quite low frequency modulation signals tend to be corrupted by the multiple scatter path lengths and by the delay in absorption and release of photons in those atoms at low energy states.

Also if continuous laser radiation is delivered to a mass of cells the high damping factor of the structure means that in general the overall temperature of the cell mass rises. This occurs even if modulated at the resonant frequency of a particular molecule. The use of laser radiation in this way produces an increase in the reactivity of the entire cell surface which means that no actual change in the reaction products occur because the cells are in general, at equilibrium.

Conversely if very low energy is delivered at the resonance frequency of the cell adhesion molecules or if energy can be delivered as an intermittent pulse of extremely short duration, the cell adhesion molecules and the integrins with their inherently high Q structure tend to maintain a slightly higher temperature than the surrounding molecules. Thus the cell adhesion molecules can be stimulated to a greater reactivity than the surrounding surface molecules.

Many biological processes can be disturbed into a cascade of increasing reactivity if an initial response is initiated. The immune response is a powerful example of this but the nature of biological reactions on the cell surface means that similar cascade reactions occur for a wide variety of initial conditions disturbed from equilibrium. Thus a very small change in the reactivity of a surface molecule for a short time can result in a dramatic change in the chemistry of the cell surface for a considerable period after the stimulation.

This effect depends on the cell chemistry being substantially in equilibrium at the commencement of the delivery of the radiation, otherwise the resonance effect will tend to be swamped by the current dominant reaction. Thus the target cells must be in a relatively neutral pH environment and obviously not engaged in a vigorous metabolic process. Ideally also the cell surface molecule would be neutral or slightly negative as this increases the absorption of photons and so increases the transfer of energy from the laser to the molecule.

Although this limits the use of this method, it has one beneficial effect with respect to therapeutic use in carcinomas. The undifferentiated cells of a carcinoma are generally at equilibrium on the surface as most of the chemical energy of the cell is

expended internally in the cell duplication process. This means that the undifferentiated cells of a carcinoma are particularly susceptible to the effect of the method on the surface chemistry since by their nature they conform to the ideal requirements for low energy disturbance of the equilibrium.

It is a critical requirement of this effect that the initial stimulation is periodic and of very low overall energy, as higher energy stimulation would merely raise the temperature of the entire cell by conduction and would not change the reaction equilibrium. To achieve such a change, individual molecules on the cell surface must be at different temperatures. Ideally it would consist of small, directed bursts of light modulated at the frequency of the desired molecule. Unfortunately it is clearly impossible to direct such a beam in the highly scattering medium of a living human body.

If a conventional laser or simple light beam is directed at a highly scattering medium, the modulation is eliminated at any substantial frequency because the light paths to any given point are so numerous and of such differing lengths that any modulation is reduced to noise after a few millimetres of the scattering medium. Even at lower frequencies the general level of overall energy delivered to the cells means that conduction and

convection tend to raise the overall temperature of the cell surface rather than allow isolated temperature differences to exist for any useful length of time. Further it is impractical to generate a light pulse which is of sufficiently short duration and with a sufficiently high pulse repetition frequency to be of practical use in the stimulation of any resonance of a Q likely to occur in a living cell surface molecule.

This invention provides a means of differentially stimulating at least those molecules susceptible by their structure to resonant stimulus.

The invention and preferred features thereof are defined in the appended claims.

Embodiments of the invention will now be described, by way of example only, with reference to the drawings, in which:

Fig. 1 is a block diagram of an apparatus embodying the invention;

Fig. 2 illustrates an interference pattern produced by the apparatus of Fig. 1;

Fig. 3 shows the same interference in a scattering medium;

Figs. 4 and 5 show typical cell adhesion molecules;

Fig. 6 shows a human integrin molecule with a single substantial high Q resonance;

Fig. 7 shows the zinc structure of the GAG protein in the HIV virus; and

Fig. 8 shows a typical laser diode spectrum.

Referring to Fig. 1, the apparatus comprises a laser diode 2 which is controlled by an amplitude modulator 1. The laser diode 2 is selected to have a reasonably linear relationship between current and wavelength with minimum mode hopping. The amplitude modulator 1 modulates the current to the laser diode 2which in turn results in a very small wavelength modulation of the laser, for purposes discussed below.

The output of the laser diode 2 is collimated by a lens 3 and passed to an optical element 4. The optical element 4 consists of a first diffraction grating, a refractive element, and a second diffraction grating such that the beam is substantially cancelled. A preferred form of the optical element 4 is as disclosed in WO97/22022 (now EP-A1-0865618A and US-A-6064500). This allows the cancellation to occur over a small percentage of the wavelength variance of the laser source, rather than at a single critical wavelength. Wavelengths beyond the acceptance bandwidth of the cancelling optic 4

above and below the centre frequency pass without being cancelled. This means that a complex Fresnel / Fraunhoffer zone will be generated, defined by the beat frequency of the high and low frequencies as a function of the aperture. This means that relatively sparse zones of constructive interference will occur between the high and low frequency passes of the cancellation element in selected directions from the aperture, as shown in Fig. 2.

As seen in Fig. 1, the optical element can be adjusted angularly between positions 4A and 4B. This varies the ratio of constructive to destructive interference.

In effect the continuous beam is transformed into a string of extremely short duration pulses typically of sub femto second duration. The small wavelength modulation of the laser diode 2 causes the constructive and destructive nodes to move rapidly through the volume of the Fresnel zone of the collimator lens aperture. This has the effect of simulating very short (sub picosecond) pulse behaviour at any point in the Fresnel zone through which the nodes pass at a pulse repetition frequency defined by the amplitude modulator frequency.

The wavelength of the cancellation and constructive interference zones for a theoretical single path

would be the difference between the two frequencies. If the bandwidth of the cancelling element is narrow this difference is very small and the effective wavelength of the cancelled / non-cancelled cycle would be very long, of the order of pico-seconds. Therefore, the system would behave substantially similarly to a system with no cancellation because it requires an aperture much larger than the primary light wavelength to generate a useful Fresnel / Fraunhoffer zone. Such an aperture would greatly multiply the available Feynman diagram paths eliminating any useful effect, even if it were possible to generate a sufficiently coherent source of such an aperture.

If the beat frequency can be made high enough the wavelength of the cancelled to non-cancelled cycle can be a fraction of a practical aperture. This will make this wavelength sufficiently small to limit the Feynman paths to within a cycle or two in free space allowing the Fresnel / Fraunhoffer effect to be apparent. Since the centre frequency and spectrum spread of a laser diode is easily modulated by adjusting the current and or temperature of the junction, the pattern of the Fresnel / Fraunhoffer zones can be varied dramatically by very small variations in the wavelength of one or both pass frequencies. Such modulation is produced in the apparatus of Fig. 1 by the amplitude modulator 2.

Ideally the diode is modulated only slightly so that the frequencies of the laser spectra move by an amount smaller than that which would cause a second lobe to spill outside the bandpass of the cancellation element. As described above the aperture of the apparatus has a dimension some substantial multiple of the wavelength of the laser and some significantly smaller multiple of the cancellation cycle. Thus the number of different Feynman diagram path lengths will be substantially less than infinite for any given cycle length. Thus as different rays from the laser take slightly different paths through the optical element and thereafter cause the complex Fraunhoffer zone within the beam the pattern generated is the inverse of a typical narrow spectrum Fraunhoffer zone.

Therefore, instead of the centre frequencies of the beam being in general uncancelled, the centre frequencies are totally cancelled. Thus instead of a general constant level of light in the beam, the beat frequency beam is characterised by isolated relatively sparse "islands" of constructive interference occurring in the generally cancelled beam. Small variations in the centre frequency of the laser as a result of modulation of the current or temperature of the diode cause these islands of constructive interference to move rapidly within the beam.

Thus at any given point within the beam path, a constructive interference node can be made to modulate with respect to the modulation frequency of the laser, irrespective of the scattering of the path to that point. This is because few areas of constructive interference exist in the initial beam and while a constructive node can occur at any point which happens to have suitable path lengths through the scattering medium to the source, the initially cancelled portion of the beam can not be reconstructed to become a constructive node at any point. Since the modulation of the laser changes the locations of the constructive nodes at the modulation frequency of the laser the result is that for any point (or more accurately for the substantial majority of points) within the beam a modulation occurs irrespective of the scattering nature of the medium. This is because the probability of a scatter from one sparse node to a region where another sparse node has existed within frequency of the modulation is extremely low.

In a typical coherent beam, the presence of constructive or destructive interference is of equal likelihood and the modulation of the beam will generally shift one constructive node only to be replaced by another causing any initial modulation of the beam to swamped by the noise of the multiple paths. In contrast, the limiting factor for the modulation frequency of a sparse constructive

interference beam is simply that the overall maximum path length of any substantial probability in the Feynman diagram. Path length is substantially shorter than the wavelength of the modulation.

For a depth of five or six centimetres in human tissue this allows frequencies in excess of 10 MHz to be successfully modulated and in many human tissues such as bone or neural tissue the depth would be substantially greater or the limiting frequency higher.

A conventional coherent or incoherent beam would have high probability paths in the Feynman diagram. These paths would overlap at very low frequencies (kHz) and be of little practical use in the stimulation of molecular resonance. It should be noted however that the phenomena described above may be used as a means to multiply the modulation frequency, up to the point where the beam effectively becomes continuous. Thus by careful selection of the aperture, the region of the beam selected for transmission through the medium and the modulation frequency it is possible to cause the constructive nodes to pass across any given point in the beam at frequencies many times higher than the modulation frequency. In ideal conditions the duration of exposure to a constructive node of any point would be for a period equivalent to a quarter

of the duration of a wavelength of the molecular frequency repeated once per cycle.

If the wavelength of the laser is chosen to be one easily absorbed by the atomic structures it is desired to induce to resonance, then the beam will efficiently deliver the desired modulation frequency to the desired molecules. The energy of the beam is extremely low but sufficiently high to differentially raise the temperature of those molecules of sufficient Q. Higher energy intensity would tend to cause sufficient scatter even from the isolated island nodes to swamp the modulation. Again the result would be a general temperature increase rather than the differential temperature increase of the desired molecules.

Higher intensity can not significantly increase the energy delivered to the desired molecules. Once the probability of a single photon absorption at any point on the molecule in a given and resonant frequency cycle is exceeded, there is little advantage in increasing the intensity since a second photon will scatter without delivering more energy to the given atom structure. The maximum temperature difference that can be induced will be a function of the damping factor and the Q of the resonant component of the molecule. Therefore, increasing the time of stimulation is pointless beyond some

reasonable multiple of the known time required to initiate the reaction desired because the maximum possible temperature variance will occur within a few seconds.

The effect is therefore, only of merit in systems where a small temperature variance can disturb the equilibrium. Naturally this limits the range of molecules that can be stimulated by this method. It is fortunate however that many of the most usefully stimulated molecules have exactly the characteristics required. Most particularly the cell adhesion molecules and integrins mentioned above. It should be noted of course that all biological reactions occur within a narrow temperature range and the progress of most reactions can be varied quite significantly by small temperature differences. It is of course a natural consequence of light stimulation of a molecular resonance that the molecular node temperature of the resonant structure will coincide with the maximum valence state of the atoms since they are in the process of absorbing and emitting photons and so the electrons are in general at a relatively high energy state. Naturally specific photochemical reactions will be favoured and this may either help or hinder the ability of the method to stimulate a specific desired reaction depending on the proximity of unwanted photochemical reaction sites to the resonant stimulated sites. In designing a specific stimulus these factors should be taken

into account along with the equilibrium state and the pH.

As stated above cell adhesion molecules and human integrins such as Alpha 4 Beta 1 are ideally suited for excitation to chemical activity by this method.

The stimulation of cell adhesion molecules and integrins moderates a number of extremely useful biological processes. Not least of these is cell adhesion itself. It is obviously beneficial to stimulate the adhesion molecules of a carcinoma as the cell adhesion of carcinomas is relatively depressed and enhancing the adhesion serves to reduce the probability of metastasis. Such an effect would be especially beneficial prior to the excision of a tumour, reducing the likelihood of surgically shedding carcinoma cells into the blood or lymph system. The cell adhesion process and the integrins especially Alpha 4 Beta 1 and Alpha 4 Beta 2 are responsible not only for adhesion but also cell recognition.

Bissel and Weaver have shown that by chemical inhibition of adhesion sites of Alpha 4 Beta1, the cell recognition can be moderated. It is therefore possible to reduce an undifferentiated carcinoma cell to its phenotype by correctly moderating the adhesion reaction. The method used by Bissel and Weaver is

practical for in vitro application and can be used as described in their patent for the measurement of response to chemotherapy but it can not practically be used in vivo. Conversely the laser radiation method can be used in vivo and because of the extremely low energies it is inherently safe at least in terms of the radiation used. Care must of course be taken to ensure that the stimulation delivered will have a desirable consequence and much work is needed to determine both the chemical responses that are most easily stimulated and which of those are desirable in a given case.

Gradually a library of reaction responses susceptible to the stimulation will be developed from theory and experiment and this library will be used to define a range of reactions that are both of clinical use and practical to stimulate. To date we have demonstrated the stimulation of adhesion in leukocytes and neural carcinomas. We have demonstrated substantial moderation of cell surface chemistry in the prostate gland.

This shows promise in the treatment of various carcinomas. Stimulation of cell adhesion and recognition alters the metabolism of the carcinoma and causes induced, spontaneous apoptosis as a result of undifferentiated cells communicating sufficiently. This in turn causes the natural apoptosis of

undifferentiated cells in an undifferentiated environment. We have substantial evidence that like Bissel and Weaver we have observed the reduction to phenotype of undifferentiated cells and leukocytes.

Wayner US5730978 has shown an integrin-moderated process which suggests that the method may have application in the treatment of auto-immune diseases and in the manipulation of the immune response in general.

In vitro, the method can be used to alter the chemistry of a variety of proteins and simple amino acid structures in a manner that may be useful in the production of pharmaceutical compounds and nutrition products. Since the polar and hydrophobic components of molecules have substantially different electron populations, Quantum Electrodynamics (QED) shows that these components differentially absorb energy from photons. Coupled with a modulation frequency close to one of the major axes of a given molecule, modulated laser stimulation can be used to increase the homogeneity of a population of proteins or simple amino acid structures. This can be highly advantageous since the metabolic absorption of amino acid structures is moderated in vivo by shape specific enzymes.

If a simple amino acid nutrient is made homogeneous the number of enzymes required to metabolise the nutrient is reduced. Again the cascade effect of cell chemistry means that such a reduction in the complexity of a particular chemical process can dramatically increase the speed of absorption sometimes by several orders of magnitude since the required enzyme population is far more rapidly manufactured. This is of critical importance in many simple amino acid nutrients since they have a limited life before they are broken down by incidental chemical effects before they can deliver the required effect to the target cells.

Under ideal conditions it will be possible to order the folding of a protein to the desired biological form by successive stimulation of suitable resonant frequencies and the differential polar and hydrophobic absorption of photons. Again the application of a suitable modulated beam to a sufficient volume of protein by conventional means would be impossible as result of the scattering of the light. The sparse constructive node beam disclosed in the present application makes the delivery of the required modulation a practical possibility. A suitable array of the disclosed sparse constructive node beams could be arranged on a conveyor passing the proteins or simple amino structures sequentially under the various modulation

frequencies designed to favour each of the desired folding steps.

Clearly much research would be required to determine what modulations would be required to produce a desired protein shape and it may be that in practice very few proteins can be usefully manipulated in this way. Such research is not within the scope of this application; rather this application discloses a method and apparatus capable of moderating aspects of the folding process of proteins in a manner that can be applied to a bulk mass for the first time. It is extremely likely that a range of practical protein structures can be generated by this method and it has been shown by experiment that a population of proteins or simple amino structures can be at least made homogeneous which as mentioned above is useful in itself.

In this regard it should be noted that the rotational polarisation of the light source would cause differential absorption of energy depending on the "handedness" of a given molecular structure. In addition, if the beam is modulated at the resonance of a given structure, it is possible to either enhance the production of one rotation of a molecule versus the other. At slightly higher energy it is possible to cause the destruction by a separate chemical process of one or other rotation by

differentiating the temperature and therefore the reactivity of one rotation versus the other. This is a particularly useful application of the method as many drugs and nutrients depend on only one form of the molecule being present.

In this case of course the maximum Feynman path must be very much shorter and so the maximum depth that rotational polarisation effects would occur would be no greater than a few millimetres in a typically scattering medium. Hitherto no simple practical method has existed to purify a population of molecules to one or other rotation. The method disclosed here provides a means of operating on bulk media to generate a homogeneous single rotation population or to allow a chemical process to preferentially destroy one rotation relative to the other in a mixed population of molecules.

The chemical consequences discussed herein of molecular stimulation by sparse constructive node techniques result primarily from the repeated acceptance and release of photons by atoms at the resonant frequency of the local atomic bonds or local structure. There is a secondary effect on certain molecular forms such as tetrahedral which can be induced to spin provided the effective pulse length is sufficiently short.

While the sparse constructive interference beam is the primary thrust of the present application, it is worth noting that the Hamiltonian solution to Maxwell's equations suggest that cancelled light, although carrying no energy in the conventional sense in that it can not interact by conventional Quantum Electrodynamics (QED) processes may have an effect on the permitivity of free space and some theorists suggest an effect on the strong nuclear force. However since it can not scatter by QED effects this has no detrimental affect on the efficiency of the sparse constructive interference modulation and it could be argued that the permitivity and nuclear absorption effect, should it exist, would tend to enhance the efficiency of the modulated frequency coupling to the molecule. It should be noted that the presence of the Hamiltonian effect has never been satisfactorily proven and many theorists discount its existence as a mere mathematical oddity, however we note it here simply to point out that the effect would tend to enhance rather than degrade the benefit of the sparse constructive in interference effect. The apparatus by its nature can therefor be used as a means of delivering such a theoretical modulated Hamiltonian "scalar" wave.

Figs. 2 to 8 illustrate elements of the foregoing in more detail.

Fig. 2 shows the sparse constructive interference effect from a 1 percent bandwidth cancellation plate of 5 mm aperture. Black represents constructive nodes.

Fig. 3 shows the same sparse constructive interference in a scattering medium showing minimal degradation of the effect and an increased path width of majority destructive interference.

Figs. 4 and 5 show typical Cell Adhesion Molecules. Both would have two primary resonances a high Q resonance between the main elements at a relatively low frequency and a higher frequency lower Q resonance between the lobes of each element. The molecule in Fig. 4 has a higher frequency resonance between the main elements as it has some backbone structure between the main elements.

Fig. 6 shows a human integrin molecule which will have a single substantial high Q resonance defined by the mass of the two main elements and the compliance of the single backbone structure between the elements. This molecule is extremely easy to resonate sufficiently to moderate reactions and was the first molecule to be successfully manipulated by the method disclosed. This allowed an in vitro demonstration of cell adhesion stimulated by laser stimulation through a sparse constructive node cancellation optical device. "Tracks" of adhered cell chains could

be generated in the beam path of the device in a population of cells with substantially reduced expression of the integrin and generally little adhesion in the absence of the beam.

Fig. 7 shows the zinc "fingerlike" structure of the GAG protein in the HIV virus. Again the molecule shows the easily resonated dual element with compliant single backbone bridge. This molecule is much smaller and requires a higher energy and resonant frequency. It was successfully resonated with 470nm light using the method disclosed. It should be noted that the chemical conditions around a small viral particle are far harder to control or predict and variable results are to be expected. Even so substantial alterations in the processes of the viral coat were observed and the viral penetration of a cell population could be substantially altered.

Fig. 8 shows a typical laser diode spectrum, with a typical cancelled portion of the spectrum and the depth of the modulation that can be induced without causing the nodes to spill outside the cancellation zone and complicate the beat frequency pattern.

Different laser designs have different resonant modes and these can be selected to obtain the most useful range for a given application. Bragg gratings can be used to stabilise the laser emission line and expand the modulation amplitude that can be used while

keeping the overall frequency shift within the required boundary. Lasers can be pulsed with short duration pulses, which will produce an isolated traverse though the frequency mode of the laser and this can be determined to a high degree of repeatability. If a Bragg grating is used with a pulse laser the resulting frequency modulated pulse will have a very high degree of control. The combination of the short laser pulse and the rapid resulting traverse of the sparse constructive nodes means that a given point in the volume in front of the laser will be exposed to extremely short (sub picosecond) duration pulses. There are several applications for such short pulses and conventional methods for short pulse generation are relatively costly.

CLAIMS

1. Apparatus for the stimulation of molecular resonance by the application of very low intensity electromagnetic radiation, comprising a laser of multiple line cavity resonance consisting of a laser diode with a collimated or near collimated beam, said beam being passed through a phase cancellation optical element having the characteristic of cancelling several of the central lines of the laser frequency while leaving the higher and lower frequencies generally uncancelled such that the beat frequency of the passed frequencies forms a pattern of interference of constructive and destructive nodes in which the diameter of the beam is set to be a sufficiently low multiple of the wavelength of the beat frequency to allow a substantial Fresnel zone to be apparent in the beam and in which an aperture is provided to select a portion of the Fresnel zone wherein a substantial majority of destructive nodes are apparent relative to the constructive nodes and in which means are provided to modulate the laser frequency.

2. Apparatus as claimed in Claim 1, wherein the laser frequency is varied by adjusting the current on a laser diode.

3. Apparatus as claimed in Claim 1 or Claim 2 wherein the laser frequency is varied by physical alteration of a secondary cavity such as a crystal provided to double the primary frequency.

4. Apparatus as claimed in any of the preceding Claims wherein the modulation frequency is a harmonic of the beat frequency.

5. Apparatus as claimed in any of the preceding Claims wherein the modulation frequency is a harmonic of a specific molecular resonance.

6. Apparatus as claimed in any of the preceding Claims wherein the aperture or angle of the beam passage through the cancellation device may be varied consequently varying the beat frequency.

7. Apparatus as claimed in any of the preceding Claims wherein the selected portion of the beam may be varied to alter the balance between constructive and destructive nodes.

8. Apparatus as claimed in any of the preceding Claims wherein the means for modulating the laser frequency is the consequential mode transition of a laser diode in pulse mode.

9. Apparatus as claimed in Claim 8 where the laser diode mode is held within bounds by reflection from a Bragg grating so that the modulation of the Fresnel zone nodes is a consequence of the Fourier transform of the pulse.

10. A method of stimulation of molecular resonance by the application of very low intensity electromagnetic radiation modulated at resonant frequencies of molecules of high Q by use of a laser of multiple line cavity resonance consisting of a laser diode with a collimated or near collimated beam, said beam being passed through a phase cancellation optical element said cancellation device having the characteristic of cancelling several of the central lines of the laser frequency while leaving the higher and lower frequencies generally uncancelled such that the beat frequency of the passed frequencies forms a pattern of interference of constructive and destructive nodes, in which method the diameter of the beam is set to be a sufficiently low multiple of the wavelength of the beat frequency to allow a substantial Fresnel zone to be apparent in the beam and in which an aperture is provided to select a portion of the Fresnel zone wherein a substantial majority of destructive nodes are apparent relative to the constructive nodes and in which means are provided to modulate the laser frequency.

11. Apparatus for the production of sub picosecond light pulses, the apparatus comprising a laser producing a collimated or near collimated beam, a phase cancellation optical element through which said beam is passed, said phase cancellation optical element being formed by the series combination of a first diffraction grating, a refractive element and a second diffraction grating, whereby a pattern of interference of constructive and destructive nodes is formed in which the diameter of the beam is set to be a sufficiently low multiple of the wavelength of the beat frequency to allow a substantial Fresnel zone to be apparent in the beam, the apparatus further including means for pulsing the laser with short duration pulses to produce for each pulse an isolated traverse through the frequency mode of the laser.

ABSTRACT (Fig. 1)

This invention provides an apparatus comprising a laser diode (2) whose wavelength is modulated by an amplitude modulator (1). The laser output is collimated by a lens (3) and passed through an optical element (4) which contains two diffraction gratings spaced by a refractive element. The resulting output contains an interference pattern which can be selected and controlled to interact with chosen molecules so as to induce molecular resonance.

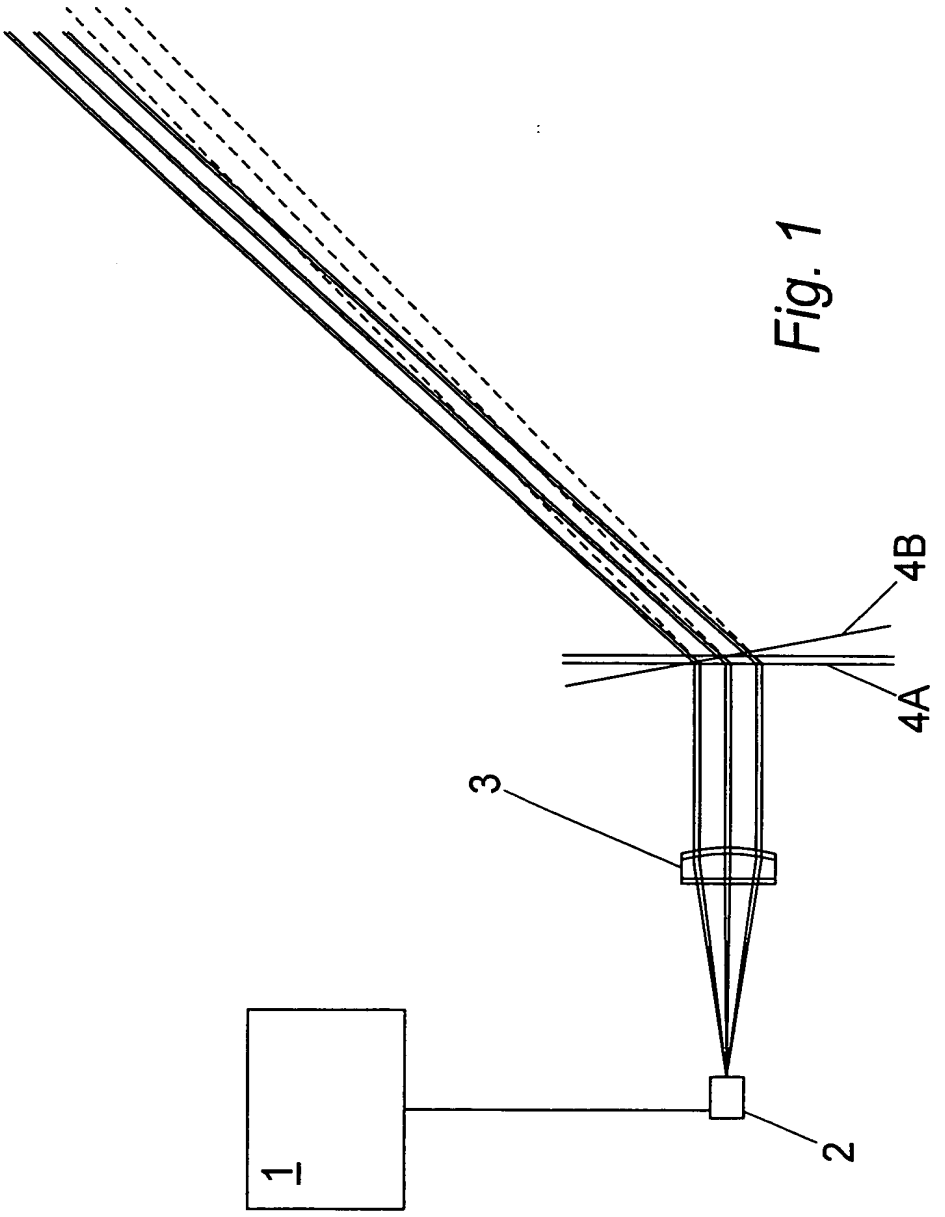

Fig. 1

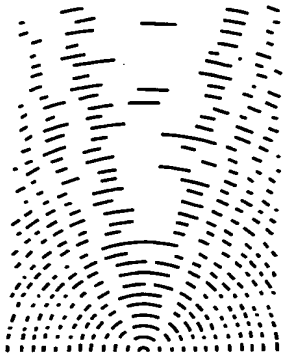

Fig. 2

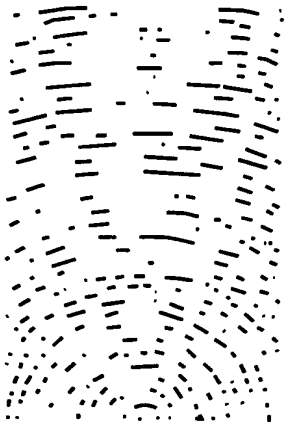

Fig. 3

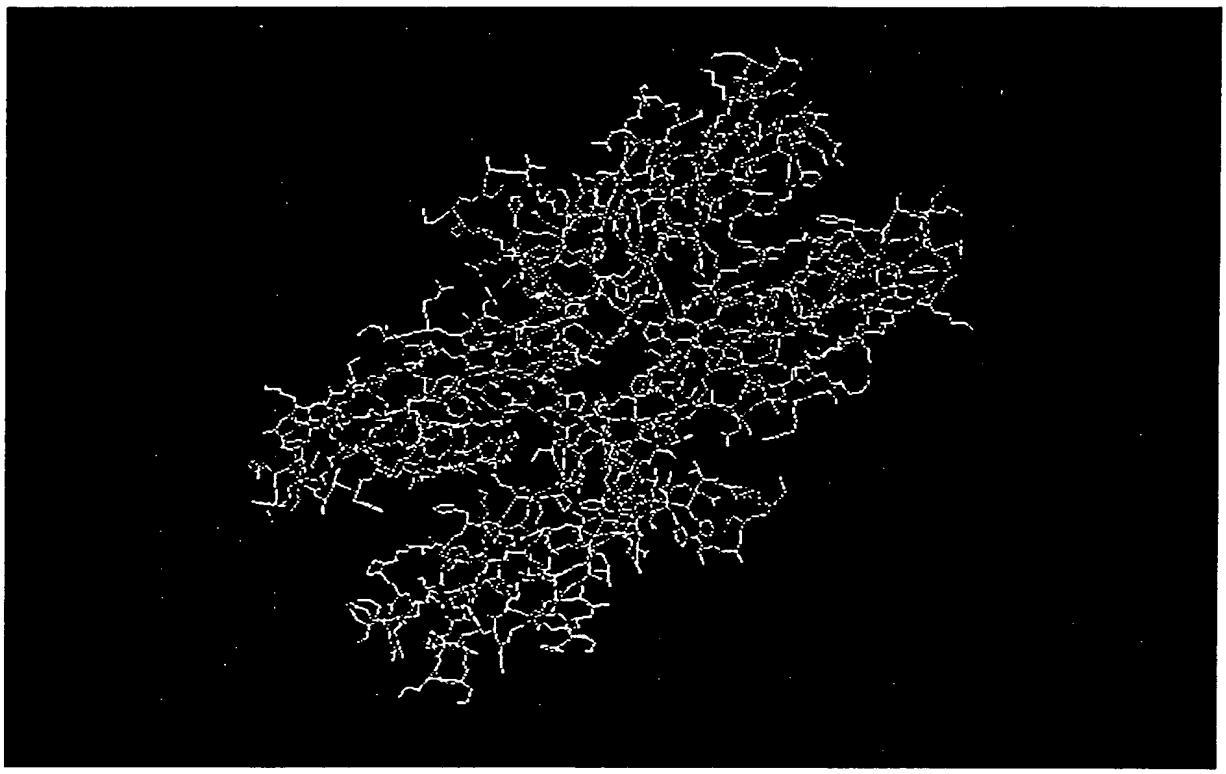

Fig. 4

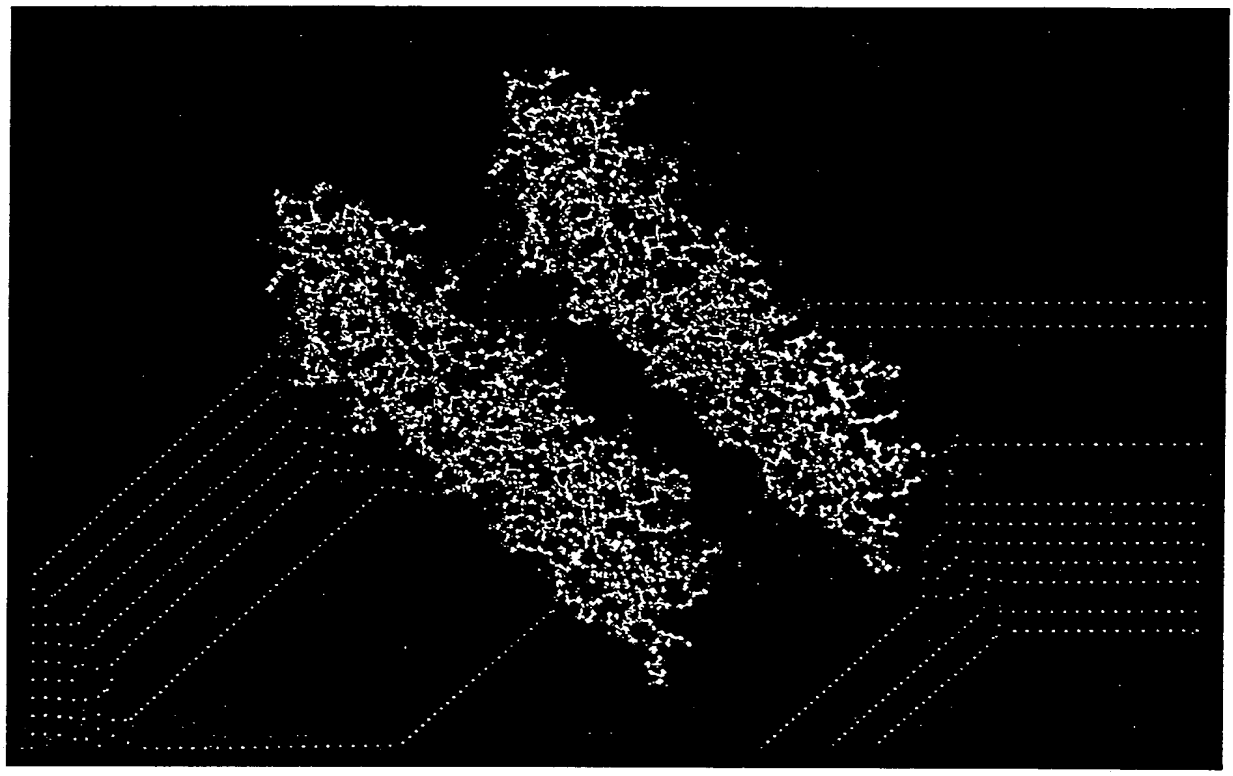

Fig. 5

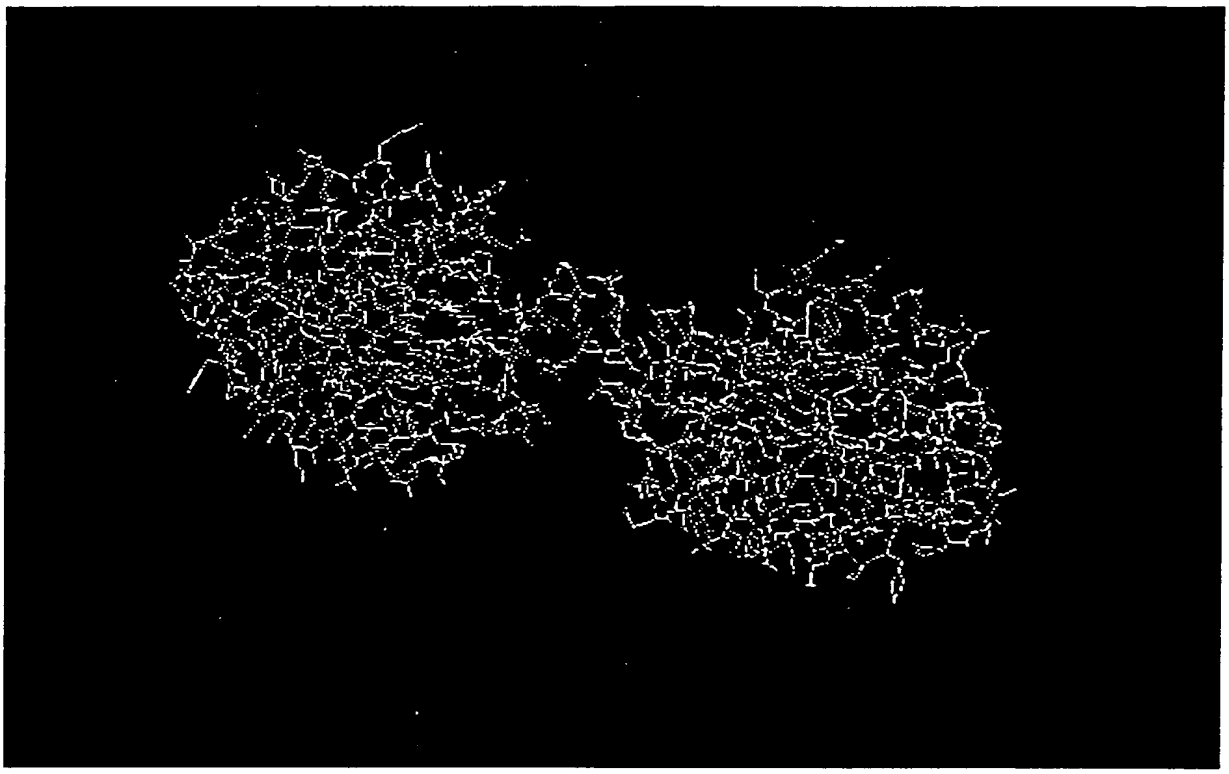

Fig. 6

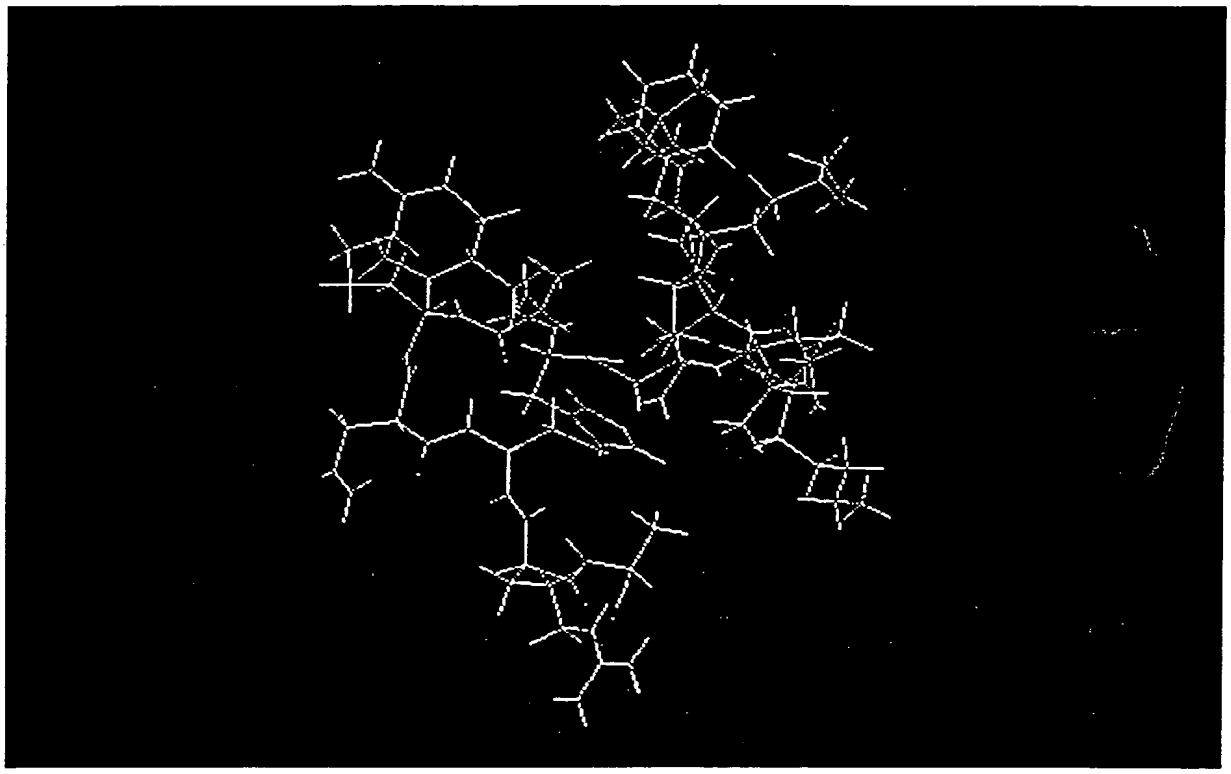

Fig. 7

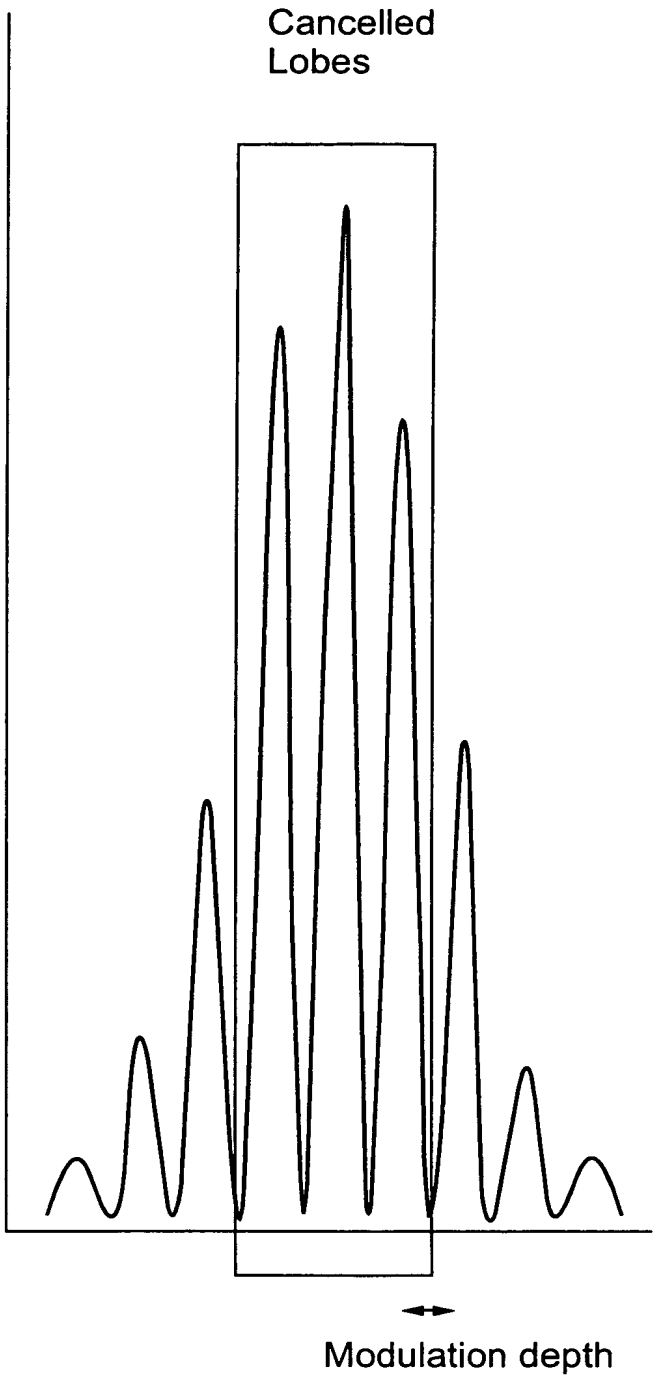

Fig. 8

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
P24404/PPP		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/03280	29/08/2000	28/08/1999
Applicant		
STRACHAN, John, Scott		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

MOLECULAR RESONANCE STIMULATED BY LOW INTENSITY LASER LIGHT

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

[X] as suggested by the applicant.

[ ] None of the figures.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

Interna[illegible]al Application No
PCT/GB 00/03280

A. CLASSIFICATION OF SUBJECT MA[illegible]
IPC 7 A61N5/067

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N G02B H01S

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 22022 A (STRACHAN JOHN SCOTT) 19 June 1997 (1997-06-19) cited in the application page 4, line 33 -page 9, line 10	1,10,11
A	US 5 658 234 A (DUNLAVY JOHN HAROLD) 19 August 1997 (1997-08-19) column 2, line 28 - line 67	1
A	US 4 834 474 A (GEORGE NICHOLAS ET AL) 30 May 1989 (1989-05-30) abstract	1,10,11
A	US 4 536 883 A (CHAPLINE JR GEORGE F) 20 August 1985 (1985-08-20) column 1, line 32 - line 50	1,10,11

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 December 2000	12/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Petter, E

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Intern...al Application No
PCT/GB 00/03280

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9722022	A	19-06-1997	AU	7704296 A	03-07-1997
			CA	2239833 A	19-06-1997
			EP	0865618 A	23-09-1998
			US	6064500 A	16-05-2000
US 5658234	A	19-08-1997	NONE		
US 4834474	A	30-05-1989	NONE		
US 4536883	A	20-08-1985	NONE		

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P24404A/AHO/PPP		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03280	29/08/2000	28/08/1999
International Patent Classification (IPC) or national classification and IPC A61N5/067		
Applicant STRACHAN, John Scott		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27/02/2001	09.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Abraham, V Telephone No. +49 89 2399 7463

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03280

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-22 as originally filed

Claims, No.:

1-11 as originally filed

Drawings, sheets:

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 1-11.

because:

   ☒ the said international application, or the said claims Nos. 10 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-9,11 are so unclear that no meaningful opinion could be formed (*specify*):
   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

III

1. According to Article 34(4)(a)(i) PCT and Rule 67.1 PCT no international preliminary examination is required to be carried out on claim 10 of the present application, because the subject-matter of this claim relates to a method for treatment of the human or animal body by therapy (see page 4, lines 16-26).

2. The set of claims does not meet the requirements of Article 6 PCT. Although claims 1 and 11 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter. The set of claims as a whole therefore lacks conciseness. Moreover, lack of clarity arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought and, consequently, no further examination of claims 1-9,11 with regard to novelty and inventive step can be carried out. The claims should have been redrafted to contain a single independent claim.

3. An examination of claims 1-9,11 with regard to novelty and inventive step is furthermore not possible, because of the following severe clarity objections:

3.1 According to the description (page 4, lines 28 -page 5, line 7) it is a critical and essential requirement of the present invention that the intensity of the electromagnetic radiation is "very low", in order to selectively stimulate desired molecules.
However, the term "very low intensity" used in claim 1 and implicitly also in claim 11 is vague and unclear, has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

Since no definition of this unclear term is to be found in the specification of the present application, the invention does not appear to be disclosed in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. Therefore, an objection according to Article 5 PCT may be raised unless the applicant proofs, that the intensity necessary for achieving the desired effect is derivable from the disclosure of the present application without the exercise of inventive skill.

3.2 Claims 1 and 11 further do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem ("the diameter of the beam is set to be **a sufficiently low multiple of the wavelength of the beat frequency to allow a substantial Fresnel zone to be apparent**"). The technical features necessary for achieving this result should be added. This does not appears to be possible, because the result itself, namely the term "substantial Fresnel zone", is vague and unclear.

Again, no clarification is to be found in the specification of the present application, and the invention does one more time not appear to be disclosed in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art. A second objection according to Article 5 PCT may be raised unless the applicant proofs, that the beam diameter necessary for achieving the desired effect is derivable from the disclosure of the present application without the exercise of inventive skill.

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
P24404/PPP		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/ 03280	29/08/2000	28/08/1999
Applicant		
STRACHAN, John, Scott		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   MOLECULAR RESONANCE STIMULATED BY LOW INTENSITY LASER LIGHT

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]GB 00/03280

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N5/067

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N G02B H01S

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 22022 A (STRACHAN JOHN SCOTT) 19 June 1997 (1997-06-19) cited in the application page 4, line 33 -page 9, line 10	1,10,11
A	US 5 658 234 A (DUNLAVY JOHN HAROLD) 19 August 1997 (1997-08-19) column 2, line 28 - line 67	1
A	US 4 834 474 A (GEORGE NICHOLAS ET AL) 30 May 1989 (1989-05-30) abstract	1,10,11
A	US 4 536 883 A (CHAPLINE JR GEORGE F) 20 August 1985 (1985-08-20) column 1, line 32 - line 50	1,10,11

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 December 2000	12/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Petter, E

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
[redacted]GB 00/03280

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9722022 A	19-06-1997	AU 7704296 A	03-07-1997
		CA 2239833 A	19-06-1997
		EP 0865618 A	23-09-1998
		US 6064500 A	16-05-2000
US 5658234 A	19-08-1997	NONE	
US 4834474 A	30-05-1989	NONE	
US 4536883 A	20-08-1985	NONE	